Session #1: Corrosion

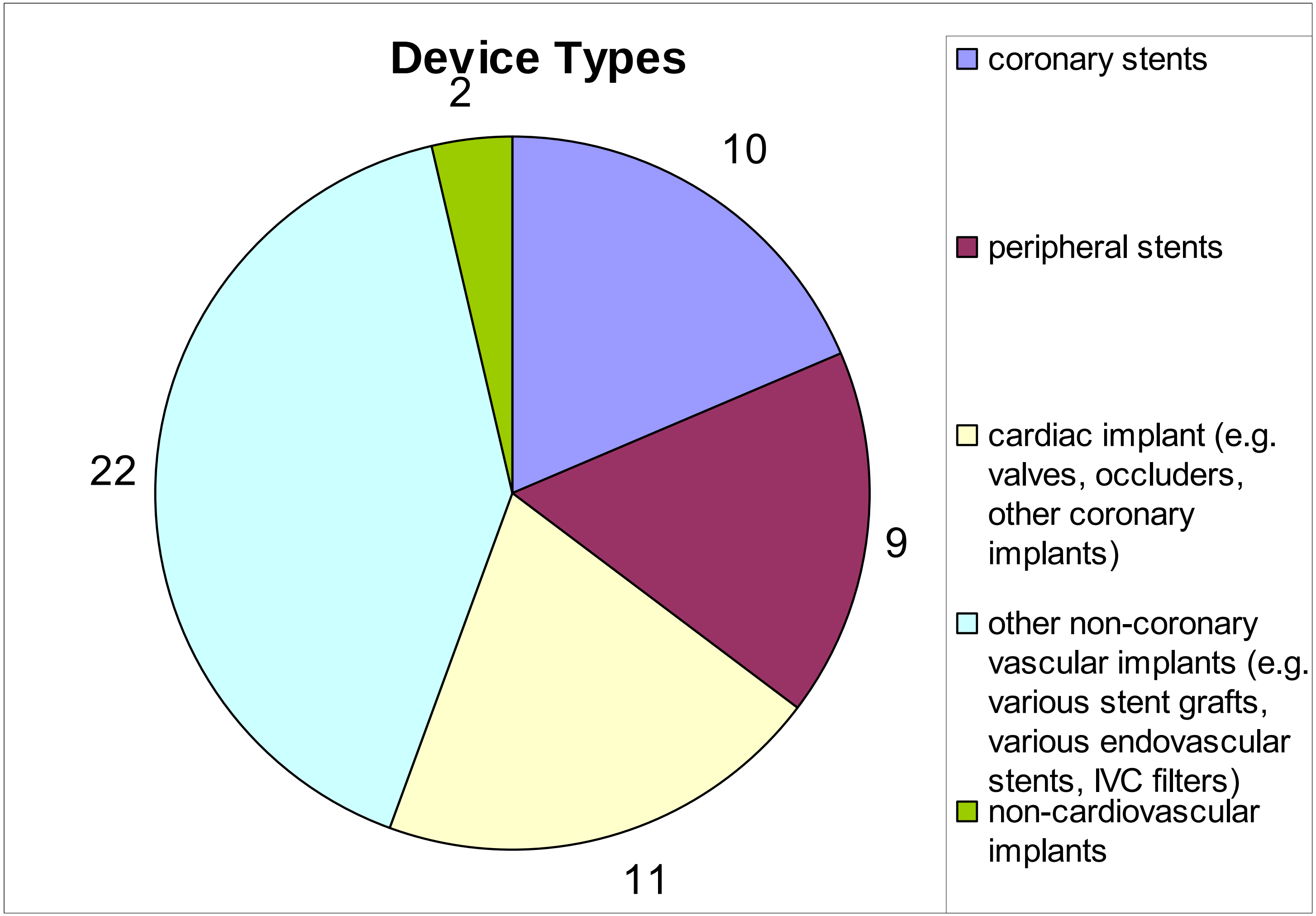
Moderator: Erica Takai, FDA

- Objective 1: Relevance of corrosion testing - Jack Lemons and Brigitta Brott (University of Alabama Birmingham; 50 min)
- Objective 2: Testing commonly performed (HW results; 5 min)
- Objective 3: What was learned from previous testing (HW results & discussion; 30 min)
- Objective 4: Acceptance criteria (HW results & discussion; 60 min)
- Objective 5: Moving forward (HW results & discussion; 90 min)

Objective 1: Describe the relevance of corrosion testing; In vivo corrosion and clinical consequences—Jack Lemons and Brigitta Brott (University of Alabama Birmingham; 50 min)

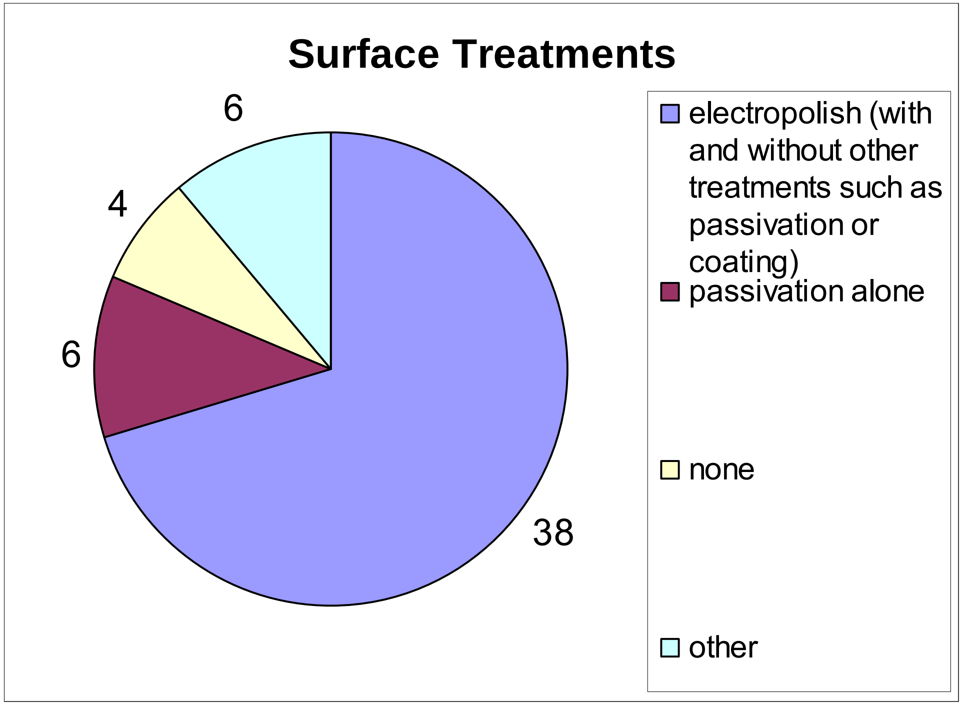
Objective 2: Identify the types of corrosion testing commonly performed (HW results; 5 min)

HW: Response demographics regarding types of corrosion testing performed

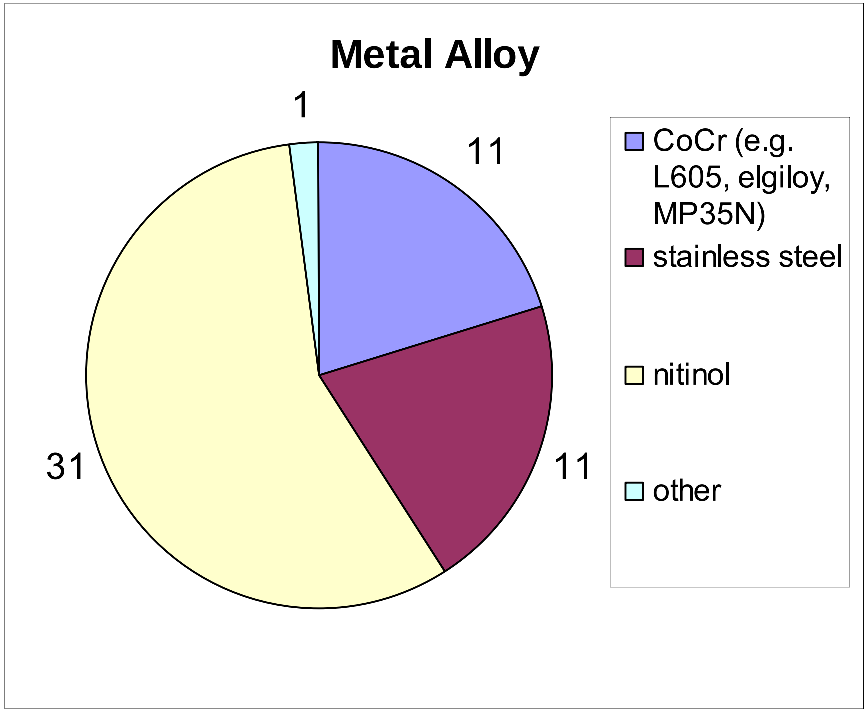


n = 54

HW: Response demographics regarding types of corrosion testing performed



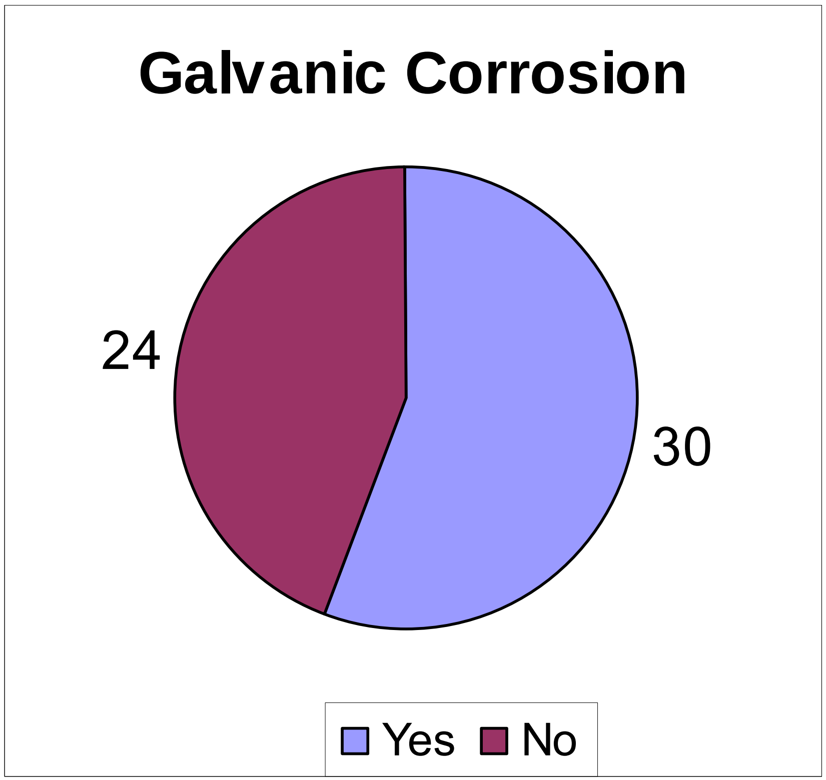
n = 54



n = 54

HW: What types of corrosion testing do you perform for cardiovascular implants?

Results from all devices and alloys pooled



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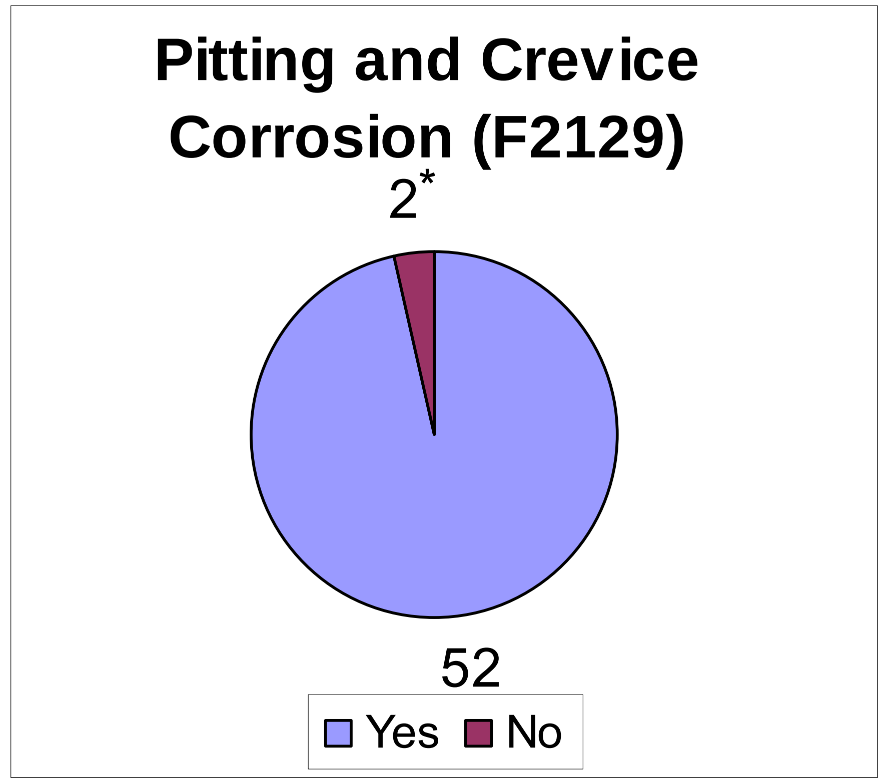
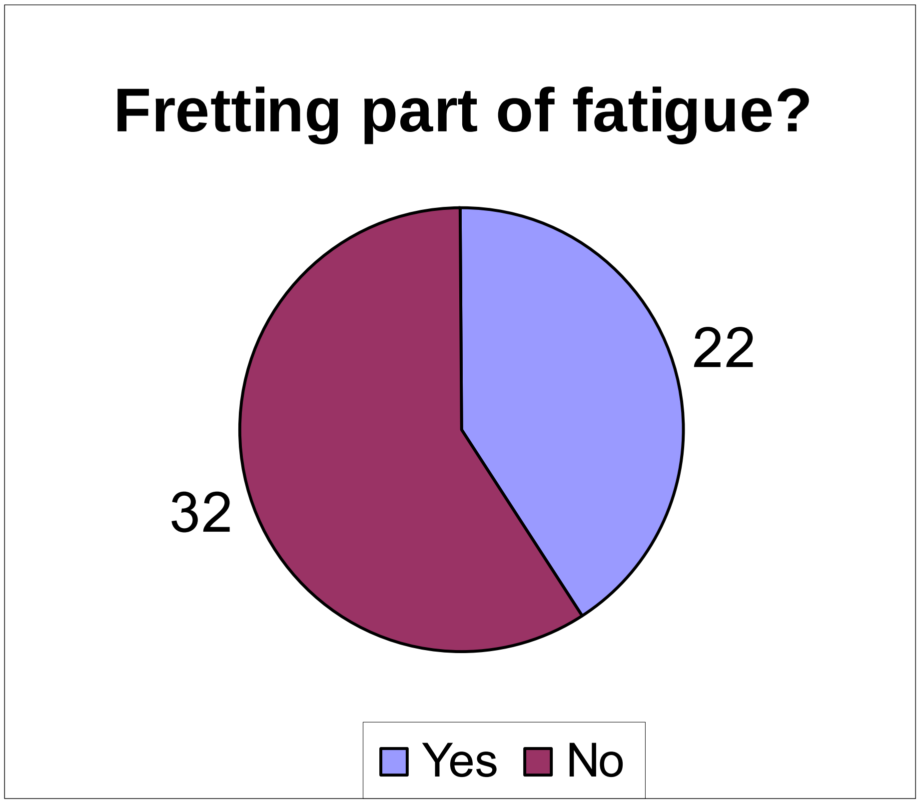


n = 54

*Note one ‘no’ response was a non-cardiovascular device

HW: What types of corrosion testing do you perform for cardiovascular implants?

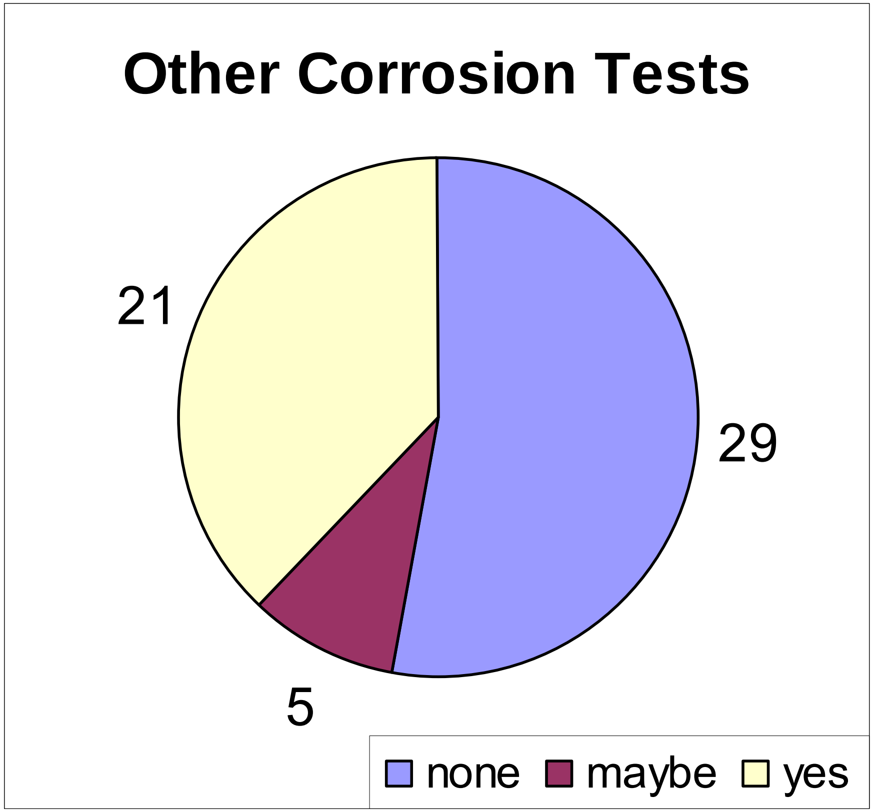
Results from all devices and alloys pooled



n = 54

n = 10 out of 54 devices reported fretting testing performed separate from fatigue

HW: What types of corrosion testing do you perform for cardiovascular implants?



n = 55

‘Yes’ responses included open circuit potential, explant analysis, and/or immersion tests

Objective 3: Identify what has been learned from previous corrosion testing; (HW results & discussion; 30 min)

HW: Please describe or identify observed corrosion events from in vitro testing (e.g. after fatigue testing) and in vivo experience (if any).

- Total respondents = 15
- In vitro: mostly none observed outside F2129 testing
  - 1 observation of corrosion post-fatigue with overlap
  - 2 observations of nickel release
- In vivo: two ‘yes’ however, one appears to be due to post-explant device handling

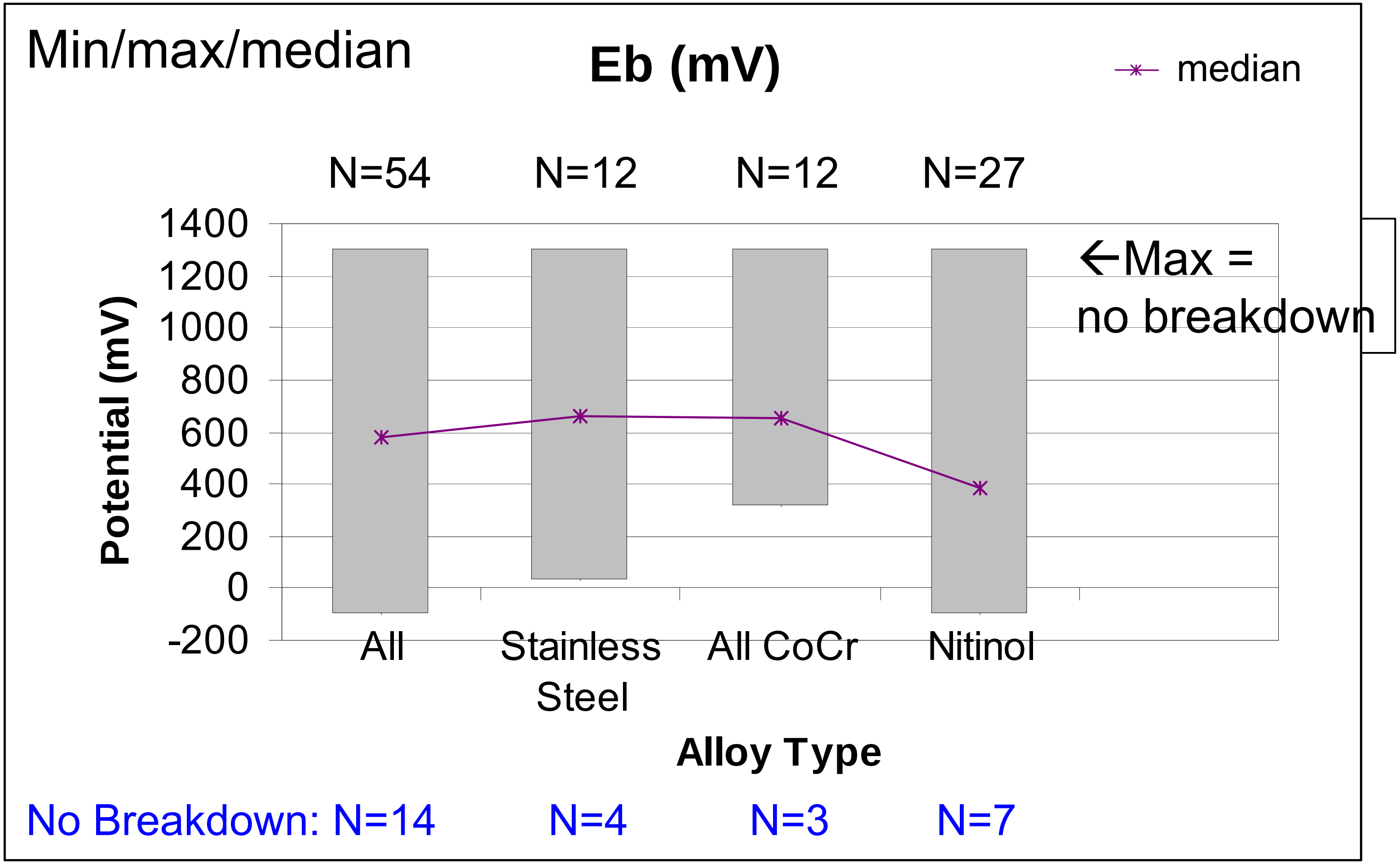
➢ Few observed in vivo events may be due to low number of returned explants for analysis or under reporting?

HW: Test parameters for ASTM F2129 testing performed

		N=68
Scan Rate (mV/sec)	**1mV/sec**	28
	0.167 or 0.2mV/sec	40
		N=64
Solution	**PBS**	59
	Other (0.9% saline, Hank's)	5
		N=68
Covering/Coating	**covered or coated**	42
	not covered or coated	26
		N=65
Crevice?	**Yes**	35
	No	30

- N=11 devices had both pre- and post-fatigue data
- In vivo corrosion observed?
  →approximately half not analyzed, half not observed

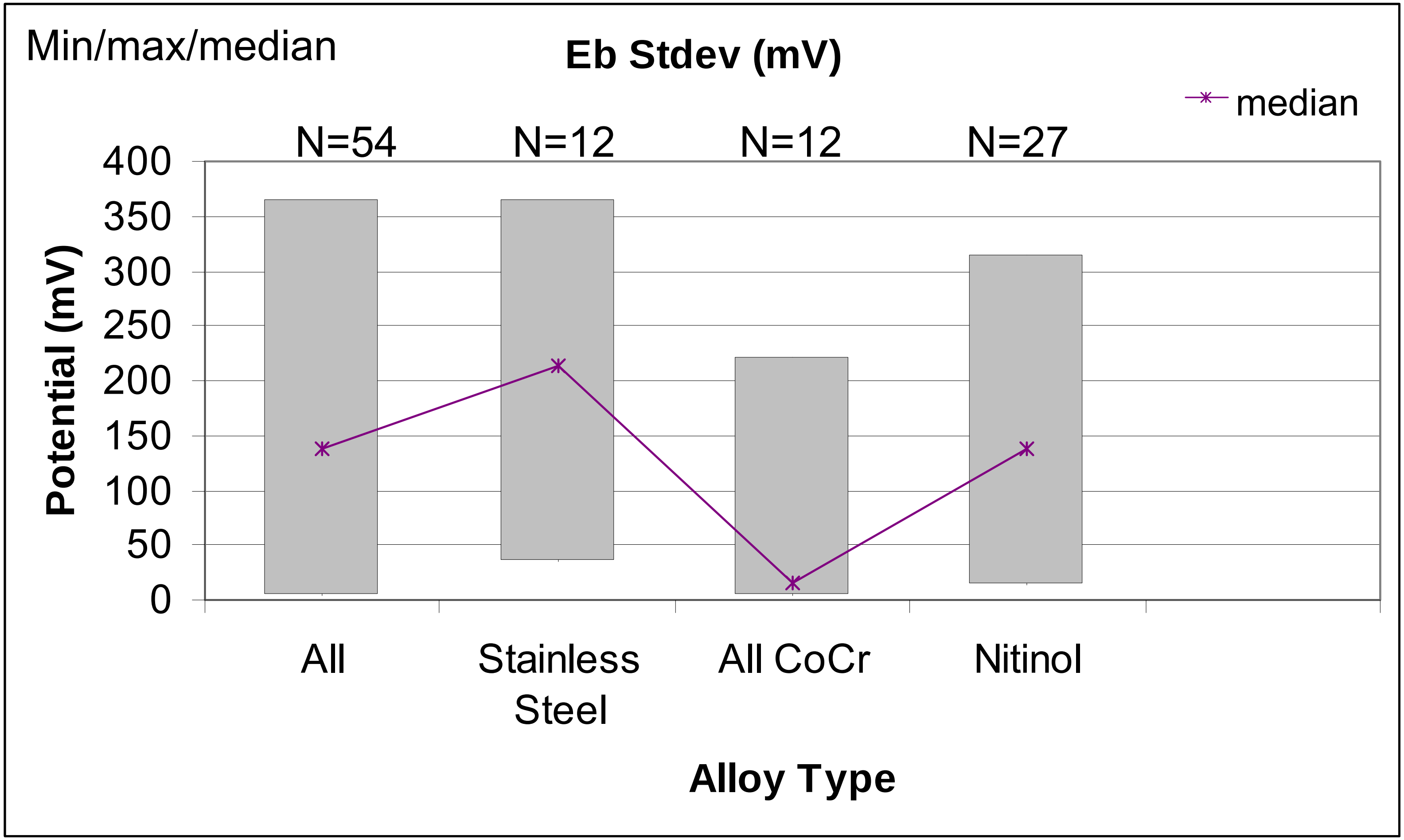
HW: Breakdown potential for ASTM F2129 testing performed (as manufactured devices):



- Median of values with breakdown

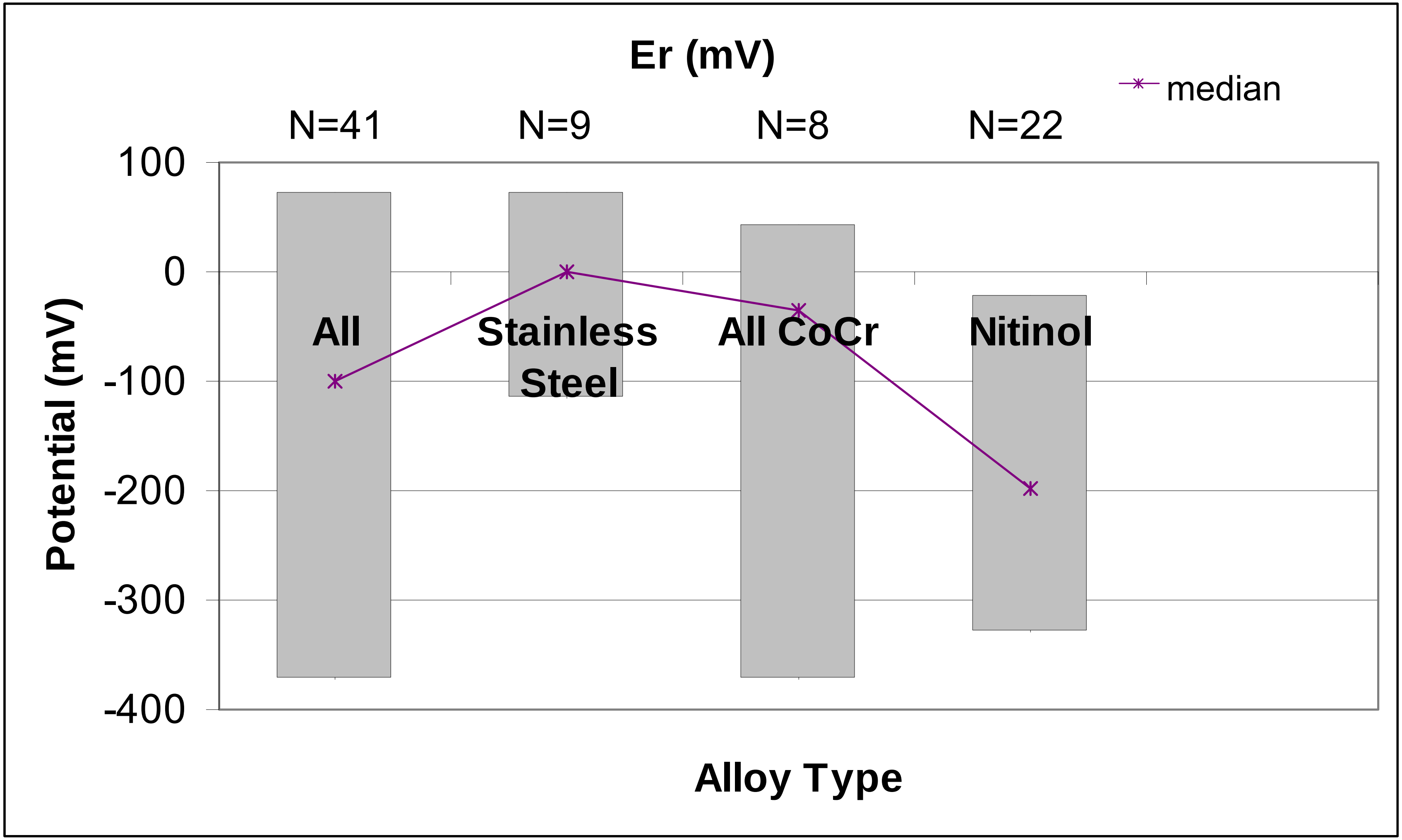
➢Generally, increase in Eb observed post-fatigue (median 583mV)

HW: Stdev reported for individual tests for ASTM F2129 testing performed (as manufactured devices)



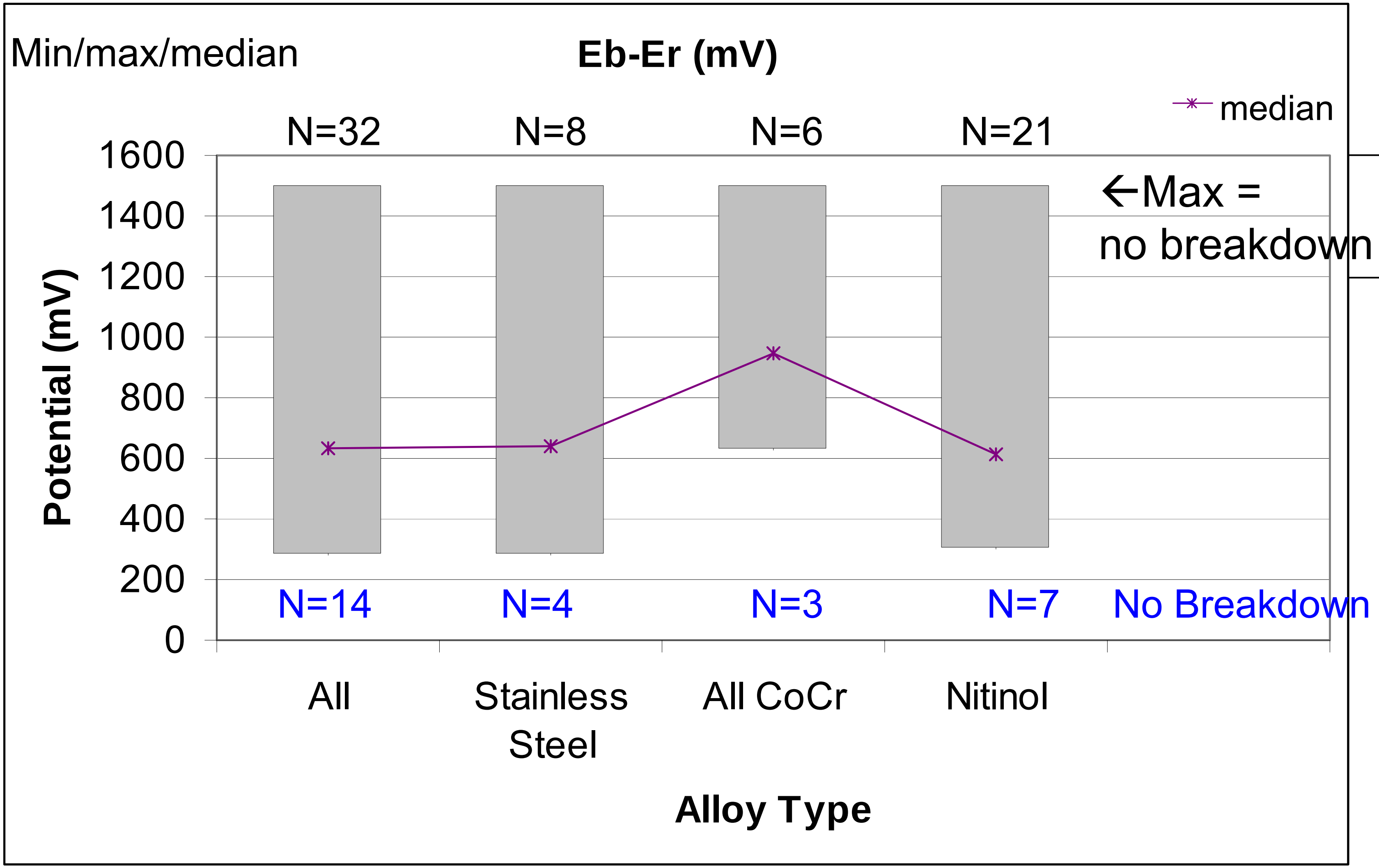
- ➢Variability within individual tests higher in stainless steel and nitinol

HW: Rest potential for ASTM F2129 testing performed (as manufactured devices):



Min/max/median

HW: Eb-Er for ASTM F2129 testing performed (as manufactured devices):



- Generally, increase in Eb-Er post-fatigue for NiTi (median 800mV)

HW: Repassivation potential for ASTM F2129 testing performed (as manufactured vs. post-fatigue devices)

	As-Manufactured				Post-Fatigue
Metal Alloy	**All**	**Stainless Steel**	**All CoCr**	**Nitinol**	**All**
Ep (mV)	N=31	N=8	N=5	N=17	N=11
none	N=18	N=6	N=3	N=8	N=5
mean	-48			-164	-73
median	-86			-100	-104
mean stdev	57			23	142
min	-331			-331	-340
max	913			50	350

- <1/2 reported an Ep
- Most reported Ep close to Er (negative #)
- Only 2 reported Ep close to Eb
- No discernable change post-fatigue

HW: If known, please identify and provide values for the in vivo driving forces for corrosion

- Hoar and Mears (1966), Proceedings, Royal Society, Series A, vol 294, p.1439.
  - Potential measured of various alloys (stainless steel, titanium, etc)
  - in goats (femoral plate) and humans (finger pin) over 71 and 90 days respectively
  - Rest potentials in the 100-600 mV range (stainless steel and nickel alloys <300mV)
  - Scratching the surfaces of the metals (in vitro) caused a transient drop in potential 1-30min.

HW: If known, please identify and provide values for the in vivo driving forces for corrosion.

- L. B. Pertile *et al.* (2009) “In vivo human electrochemical properties of a NiTi-based alloy (Nitinol) used for minimally invasive implants.” J Biomed Mater Res 89A, p.1072–1078.
  - OCP of nitinol wires in femoral, iliac and abdominal arteries
  - 6 patients during vascular surgery (measured over ~12min)
  - -334 ± 30 mV/SCE (similar to in vitro measurements)

HW: If known, please identify and provide values for the in vivo driving forces for corrosion

- Shih *et al.* (2000) “Increased corrosion resistance of stent materials by converting current surface film of polycrystalline oxide into amorphous oxide.” Biomed Mater Res, 52, p. 323-332.
  - Nitinol and 316L stainless steel wires with polycrystalline (PO) or amorphous oxide (AO)
  - Implanted in abdominal aorta of dogs, OCP 6hrs
  - -370mV (PO) vs -20mV (AO) for 316L
  - -330mV (PO) vs -30mV (AO) for nitinol

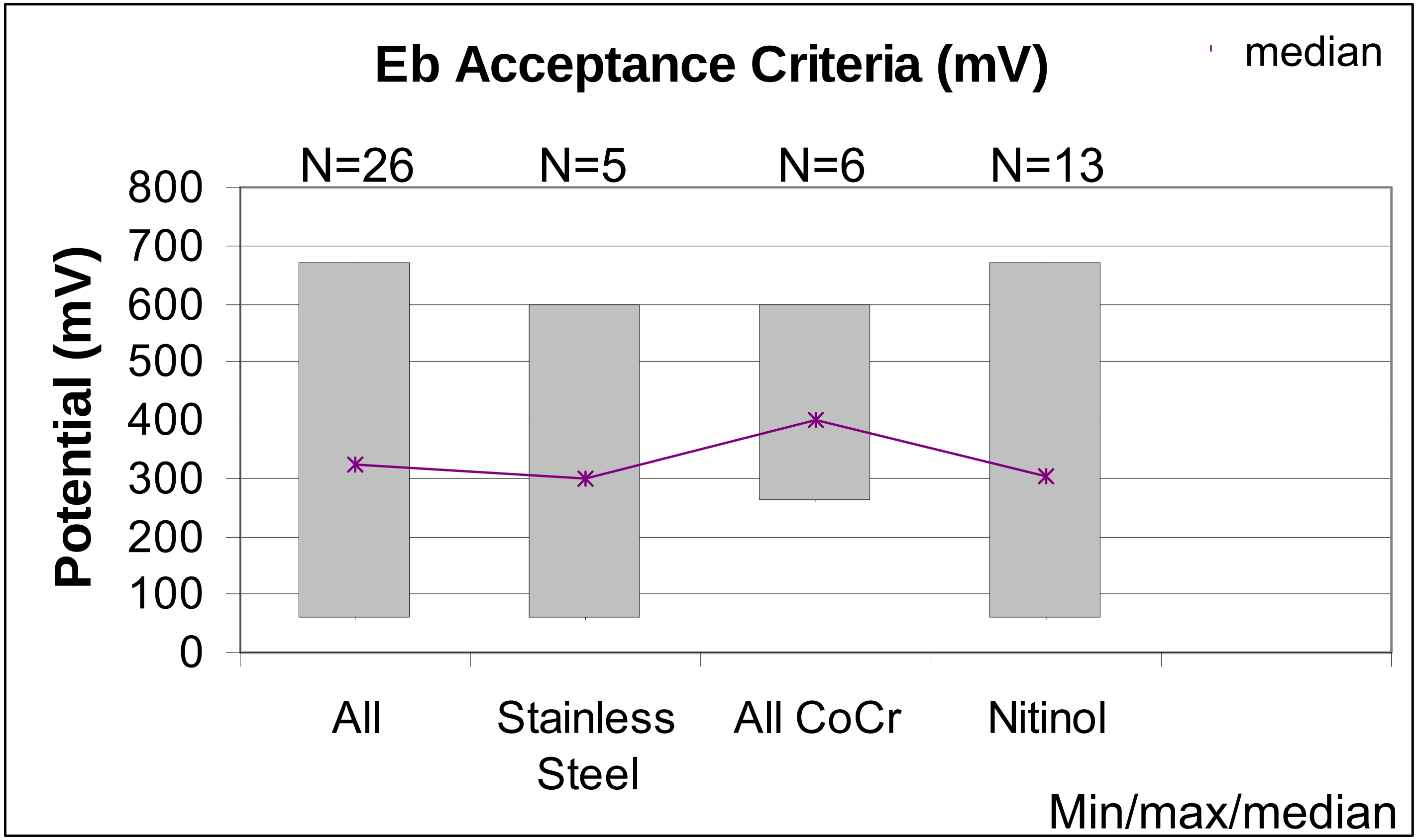
- Nerve cell conduction in ~-10-40mV range

Objective 3. Identify what has been learned from previous corrosion testing (20 min)

- 3.1. Discuss whether corrosion testing has been predictive of in vivo corrosion (from animal studies or patient explants; 15 min)
- 3.2. Identify the in vivo driving forces for corrosion (5 min)

Objective 4: Discuss interpretation of results and proposed acceptance criteria for ASTM F2129 (HW results & discussion; 60 min)

HW: What parameters do you establish acceptance criteria for / what are those criteria?



- N=3 nitinol indicated no Eb acceptance criterion
- 23 of 26 indicated no Er acceptance criterion

HW: What parameters do you establish acceptance criteria for / what are those criteria?

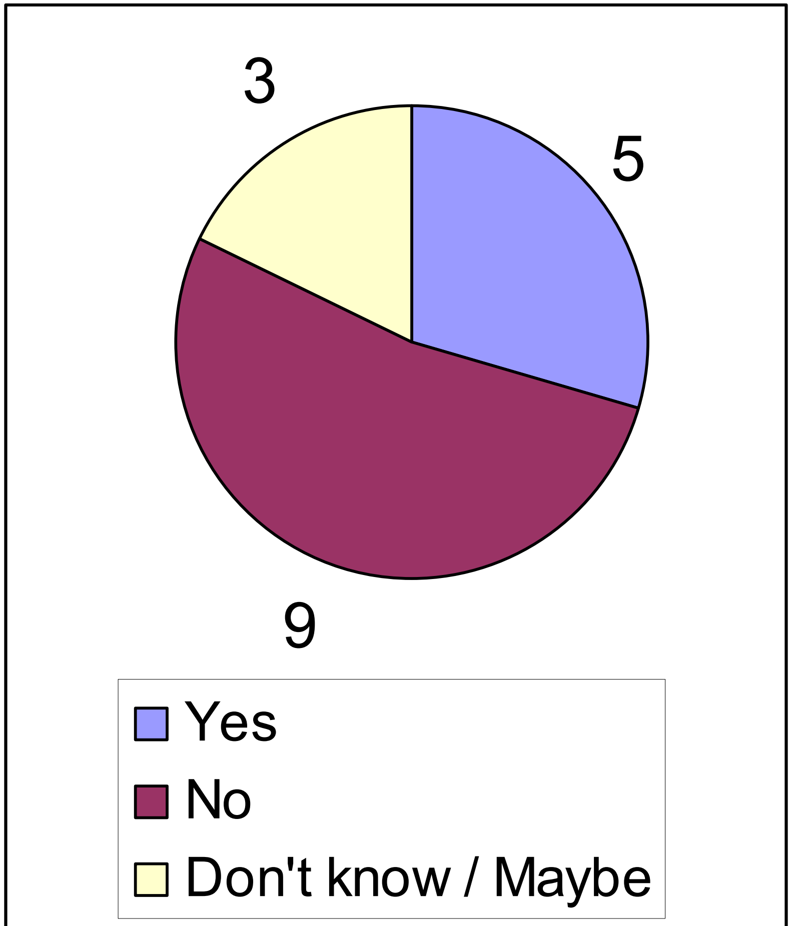
Nitinol

Eb-Er	N=13
none	N=7
median	600
min	200
max	718.3

- 16 of 26 indicated no Eb-Er acceptance criterion

- Some responses both with and without set acceptance criteria indicated that they compared results with another marketed device (n = 8)
- Some set acceptance criteria as ‘average value’ with no more than 1-2 samples below a set minimum value (n = 3)

HW: Is it appropriate to use universal acceptance criteria (across device types and alloys) for ASTM F2129 testing?



n = 17

- Eb-Er might be appropriate but Er varies between alloys
- F2129 results not correlated with in vivo outcomes; need to also consider intended use/location etc.

Objective 4. Discuss interpretation of results and proposed acceptance criteria for ASTM F2129 (55 min)

- 4.1. Discuss value of Eb-Er vs Eb as acceptance criteria (15 min)
- 4.2. Discuss whether specific Eb or Eb-Er values are universally appropriate (20 min)
- 4.3. Discuss the significance of Ep (10 min)
- 4.4. Discuss any other corrosion testing concerns (10 min)

Thought experiment (objective 4):

- When comparing to a predicate device, when Eb results are the same, but Eb-Er is poorer, is this acceptable?

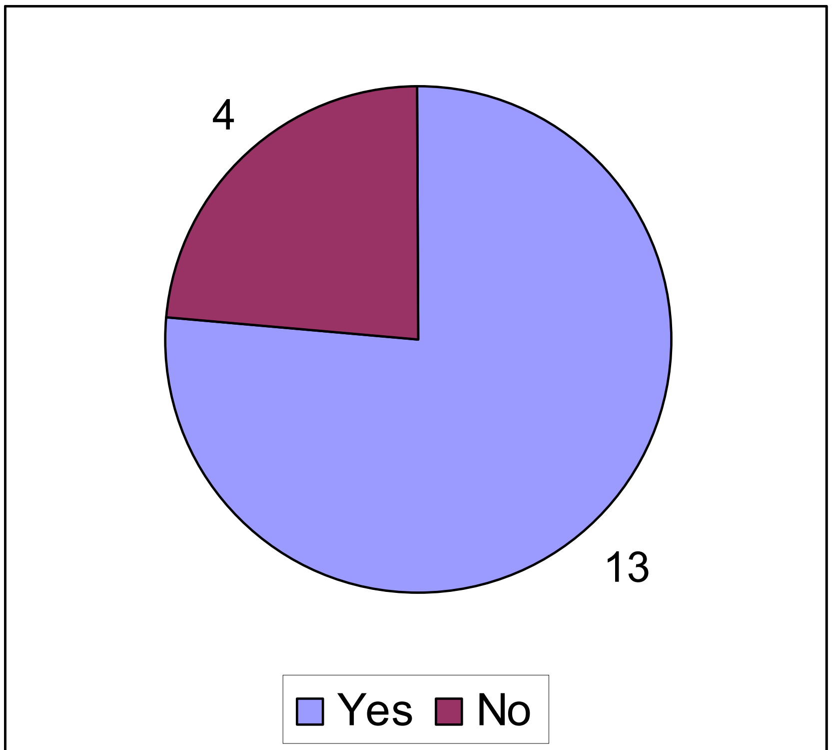
- What if Eb is poorer but Eb-Er is better?

Objective 4. Discuss interpretation of results and proposed acceptance criteria for ASTM F2129 (55 min)

- 4.1. Discuss value of Eb-Er vs Eb as acceptance criteria (15 min)
- 4.2. Discuss whether specific Eb or Eb-Er values are universally appropriate (20 min)
- 4.3. Discuss the significance of Ep (10 min)
- 4.4. Discuss any other corrosion testing concerns (10 min)

HW: Do you have concerns about other limitations of current corrosion test methods?

Responses mainly regarding F2129



n = 17

- Fine as a screening tool but no correlation to *in vivo* outcomes
- Lack of calibration criteria (variability across runs due to test setup)
- Effects of solution (lack of pH fluctuations, composition, de-aeration)

Objective 4. Discuss interpretation of results and proposed acceptance criteria for ASTM F2129 (55 min)

- 4.1. Discuss value of Eb-Er vs Eb as acceptance criteria (20 min)
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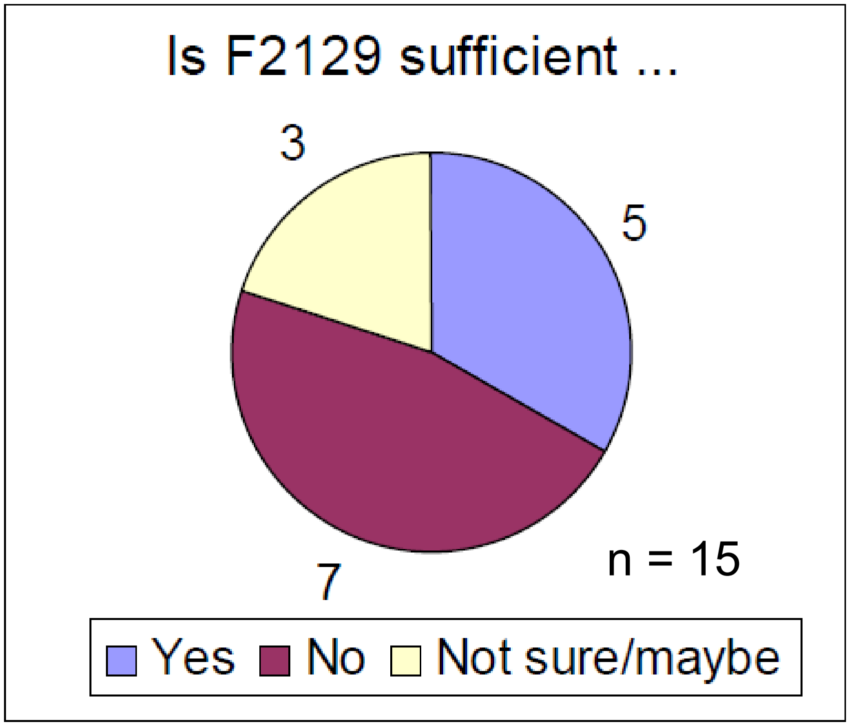
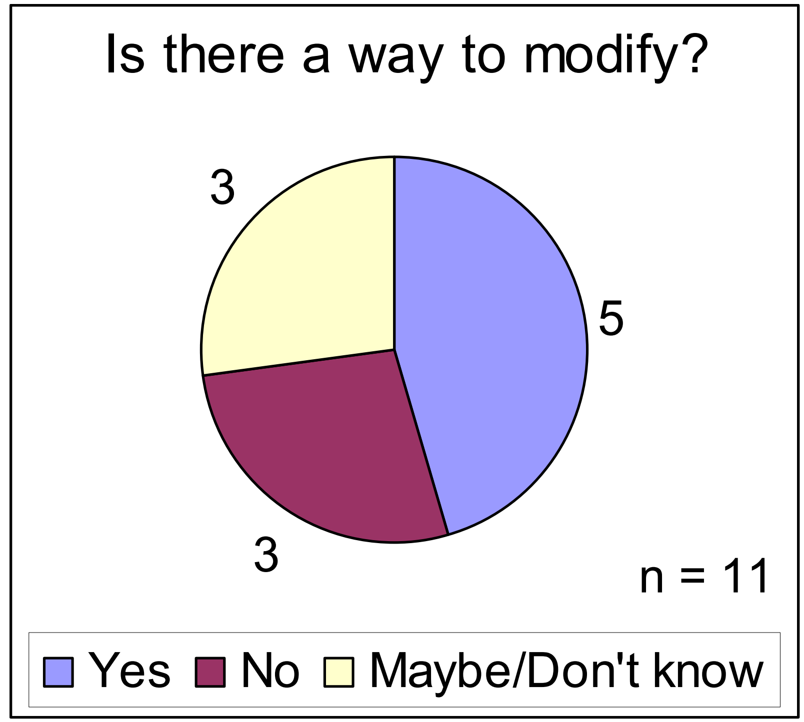
- 4.4. Discuss any other corrosion testing concerns (10 min)

Objective 5. Moving Forward: Discuss how corrosion should be assessed moving forward (HW results & discussion; 90 min)

ASTM F2129 as an assessment of clinically relevant corrosion (40 min)

HW: Is ASTM F2129 a sufficient assessment of clinically relevant corrosion?





- Only 1 response suggesting to replace F2129 with other tests

HW: Is there a way to modify?

- Need for correlation to *in vivo* outcomes

- Good for general indication of corrosion resistance but insufficient assessment alone (e.g. add fretting assessment, nickel leach testing)

- Potentiodynamic polarization curves should be assessed more deeply (e.g. Tafel characteristics, repassivation, active pitting, pitting propagation)

Objective 5. Moving Forward: Discuss how corrosion should be assessed moving forward

- 5.1. Discuss whether ASTM F2129 is a sufficient assessment of clinically relevant corrosion (10 min)
  - 5.1.1. If not (30 min):
    - 5.1.1.1. Discuss whether it is possible to modify F2129 to be more clinically relevant (e.g. acceptance criteria)
    - 5.1.1.2. Discuss what is a sufficient assessment of clinically relevant corrosion

    → Other standard test methods to evaluate corrosion (e.g. ISO 16429 and 10993-15)?
- 5.2. Potential modifications to current testing methodologies and assessments (25 min)

  → F2129:
    - Issues surrounding post-fatigue F2129 testing?
    - Others?
- 5.3. Discuss the utility of galvanic corrosion testing (25 min)

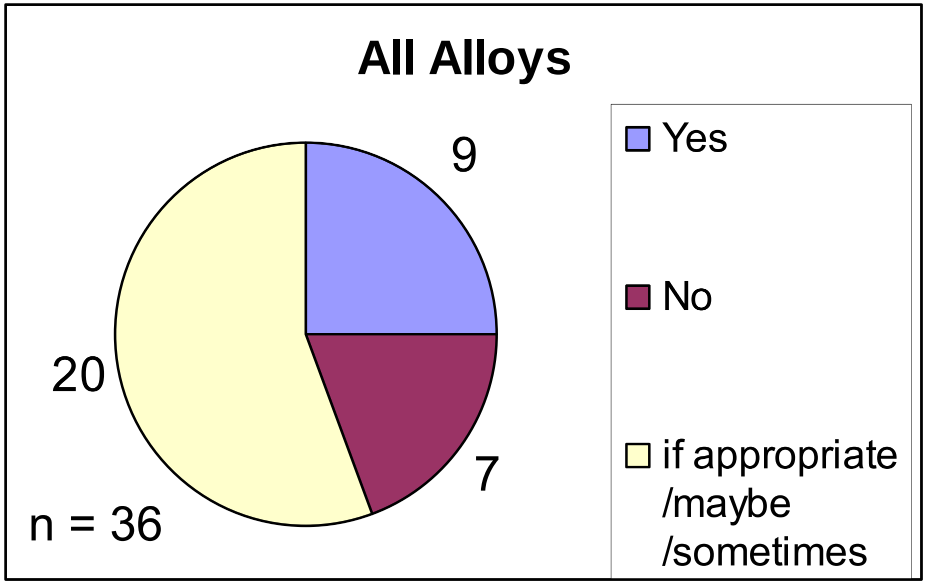
  → Modifications to galvanic corrosion testing?

HW: What is a sufficient assessment of clinically relevant corrosion?

- F2129 (comparable to predicate devices with acceptable clinical history) + other assessments
- Biocompatibility + 3-6 months animal studies (thrombogenicity and histopathology) + SEM and Auger to check for the passivation layer uniformity and thickness
- Fatigue test (with fretting for a few months) + galvanic corrosion
- Device integrity at expected life

Potential modifications to current testing methodologies and assessments (25 min)

HW: Best practices for F2129 testing: Do you use a control?

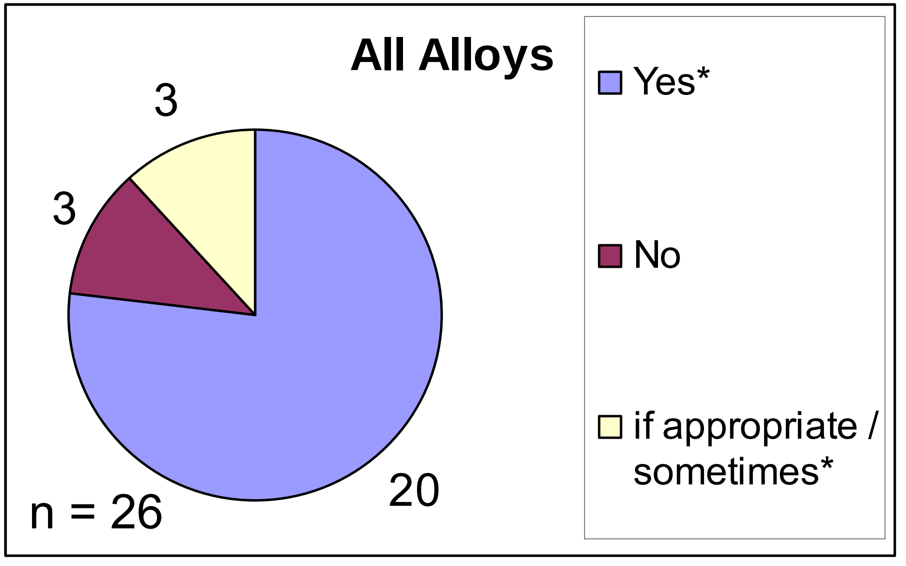


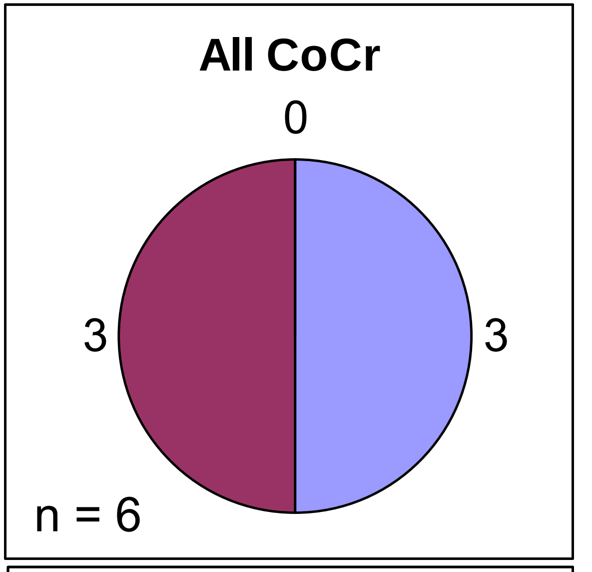
Yes = Predicate device

How many samples do you use per test?

Metal Alloy	All	Stainless Steel	All CoCr	Nitinol
# Responses	39	8	10	20
Median	6	7	5	10

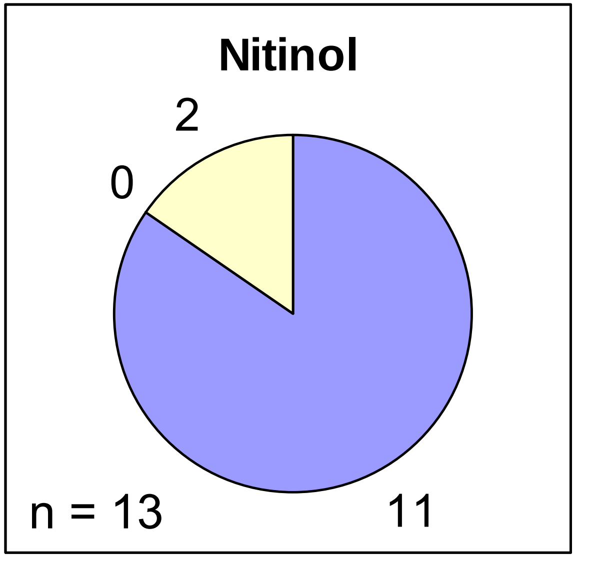
HW: Best practices for F2129 testing: Do you induce damage to the covering?





*Damage induced mainly by simulated use (with and without fatigue), one response intentionally scratched

- All n = 6 stainless steel indicated "Yes"



Objective 5. Moving Forward: Discuss how corrosion should be assessed moving forward

- ❖ 5.1. Discuss whether ASTM F2129 is a sufficient assessment of clinically relevant corrosion (10 min)
  - ❖ 5.1.1. If not (30 min):
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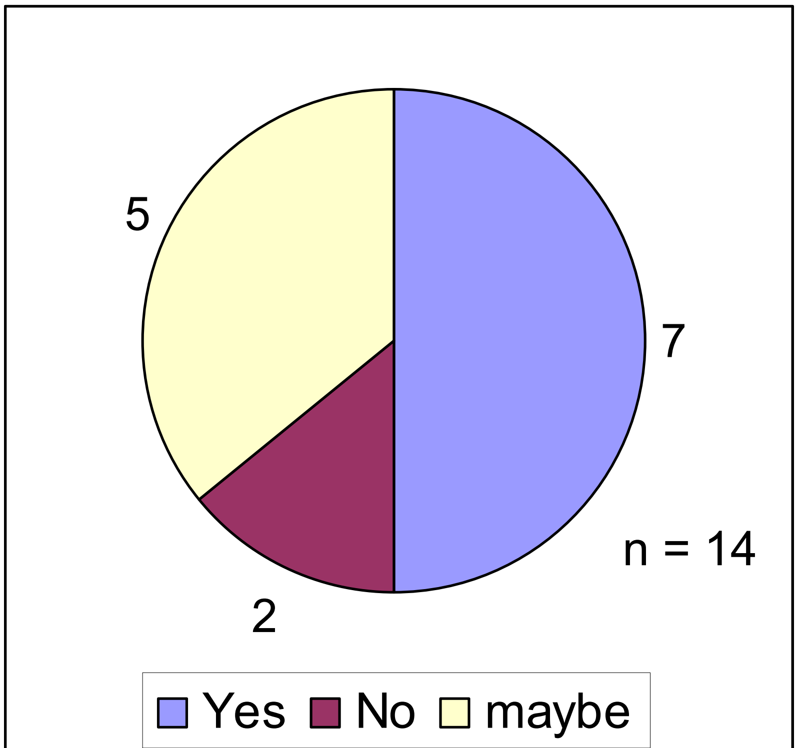
  - Issues surrounding post-fatigue F2129 testing?
  - Others?
- ❖ 5.3. Discuss the utility of galvanic corrosion testing (20 min)

  → Modifications to galvanic corrosion testing?

Galvanic corrosion testing (25 min)

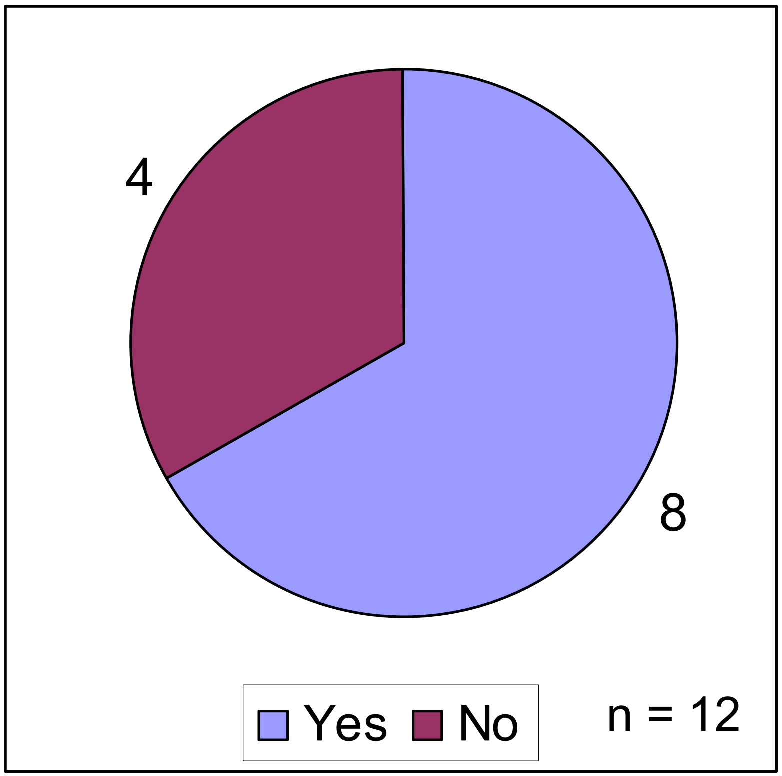
HW: Under what conditions do you believe galvanic corrosion testing is needed?

➢Is galvanic corrosion testing needed if ASTM F2129 results are “good” for a single device containing dissimilar metals?



- F2129 does not evaluate galvanic corrosion (so always should be considered)
- But if materials close in galvanic series (and cathode:anode ratio small) may not be needed
- Confirmatory test

HW: Do you believe there is value in galvanic corrosion testing of overlapped devices of dissimilar metals?



- Yes: if overlap with another device is reasonably likely to occur during clinical use
- Yes: effects of localized transient behavior
- No: Difficulty in determining/ obtaining other device
- No: Most alloys used in devices close together galvanic series (?)

HW: Best practices for galvanic corrosion testing of a single device containing dissimilar metals

Do you measure the uncoupled potential before and after?	n = 15
Yes	n = 5
No	n = 5
Only before	n = 5
Do you monitor the coupled potential?	n = 14
Yes	n = 11
No	n = 3
What is the endpoint of your test?	n = 14
Time	n = 12
Steady state current	n = 2
Do you perform testing on as-manufactured devices?	n = 14
yes	n = 13
no	n = 1

Time = 12-48 hrs

(one 4-6 day)

'No' response has not started testing

HW: Best practices for galvanic corrosion testing of a single device containing dissimilar metals

What acceptance criteria do you use for steady state current? (n=12)

- ≤ 3nA/cm^2 (n = 3)
- 2-4 nA/cm^2 (n = 1)
- Mass loss (n = 2)
- None (n = 6)

How many samples do you use per test? (n=13)

- Median = 5

Objective 5. Moving Forward: Discuss how corrosion should be assessed moving forward

- 5.1. Discuss whether ASTM F2129 is a sufficient assessment of clinically relevant corrosion (10 min)
  - 5.1.1. If not (30 min):
    - 5.1.1.1. Discuss whether it is possible to modify F2129 to be more clinically relevant (e.g. acceptance criteria)
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    → Other standard test methods to evaluate corrosion (e.g. ISO 16429 and 10993-15)?
- 5.2. Potential modifications to current testing methodologies and assessments (25 min)

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    - Others?
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  → Modifications to galvanic corrosion testing?